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beta-Sitosterol, beta-Sitosterol Glucoside, and a Mixture of beta-Sitosterol and beta-Sitosterol Glucoside Modulate the Growth of Estrogen-Responsive Breast Cancer Cells In Vitro and in Ovariectomized Athymic Mice

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Abstract

We hypothesized that the phytosterols beta-sitosterol (BSS), beta-sitosterol glucoside (BSSG), and Moducare (MC; BSS:BSSG = 99:1) could modulate the growth of estrogen-dependent human breast cancer cells in vitro and in vivo. The present study evaluated the estrogenic and antiestrogenic effects of BSS, BSSG, and MC (0.001 to 150 micromol/L) on the proliferation of Michigan Cancer Foundation 7 (MCF-7) cells in vitro. Both BSS (>1 micromol/L) and MC (>50 micromol/L) increased MCF-7 cell proliferation. Treatment with 150 micro mol/L of BSS and MC increased cell growth by 2.4 and 1.5 times, respectively, compared to the negative control (NC) group. However, BSSG had no effect at the concentrations tested. The effects of dietary BSS, BSSG, and MC on the growth of MCF-7 cells implanted in ovariectomized athymic mice were also evaluated. Estrogenic effects of the phytosterols were evaluated in the NC, BSS, BSSG, and MC treatment groups, and antiestrogenic effects were evaluated in the 17 beta-estradiol (E(2)), E(2) + BSS, E(2) + BSSG, and E(2) + MC treatment groups. Mice were treated with dietary BSS (9.8 g/kg AIN93G diet), BSSG (0.2 g/kg diet), or MC (10.0 g/kg diet) for 11 wk. Dietary BSS, BSSG, and MC did not stimulate MCF-7 tumor growth. However, dietary BSS, BSSG, and MC reduced E(2)-induced MCF-7 tumor growth by 38.9% ($P < 0.05$), 31.6% ($P = 0.08$), and 42.13% ($P < 0.05$), respectively. The dietary phytosterols lowered serum E(2) levels by 35.1, 30.2, and 36.5% in the E(2) + BSS, E(2) + BSSG, and E(2) + MC groups, respectively ($P < 0.05$), compared to that of the E(2) treatment group. Estrogen-responsive pS2 mRNA expression in tumors did not differ among groups, but expression of the antiapoptotic marker B-cell lymphoma/leukemia-2 (bcl-2) in tumors from the E(2) + MC group was downregulated, compared to that of the E(2) treatment group. In summary, BSS and MC stimulated MCF-7 cell growth in vitro. Although BSSG comprises only 1% of MC, BSSG made MC less estrogenic than BSS alone in vitro. However, dietary BSS and MC protected against E(2)-stimulated MCF-7 tumor growth and lowered circulating E(2) levels.

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